Genetics Department University of Wisconsin Madison 6, Wis.

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Dear Dr. K.-Nobel

I am delighted at your evident interest in the K-12 cultures, and wish you good luck with them.

As to lactose-mutabile cultures, I am sending you two cultures which illustrate the phenomenon very well. Y-87 is a mutant of E. coli K-12, derived from the 58-161 which you already have, in two additional steps, V_1^r (phage-resistance) and the relatively unstable Lac- mutation that gives the culture its "mutabile" character. The mutant, briefly mentioned in my 1947 Genetics paper, was obtained from a suspension treated with nitrogen-mustard. Lest you regard this "mutabile" cultures as a laboratory artefact, and therefore unsuitable for your purposes, I am also sending "ML", isolated by and from A. Lwoff, and used by him and his colleagues at the Pasteur Institute for a number of experiments (See, e.g., Monod 1947 Growth 11:223, The phenomenon of enzymatic adaptation; and especially, Monod et Audureau, Ann. Inst. Pasteur, 72:868, 1946).

In agreement with these authors, I would suggest that the papillae developing on lactose agar are simply "reverse"-mutations for the capacity to ferment lactose. In "ML" we do not have the original Lac+ form to compare with the presumed reversions, but in Y-87 a very complete analysis was made by my wife for her doctoral dissertation. Her experiments showed clearly that the papillae were indeed reverse-mutations. Irrefutable evidence on the role of lactose in securing papillae is difficult to obtain, but we found nothing incompatible with the notion that the reversions are simply spontaneous mutations, occuring at a moderate rate (about once per million cell divisions). They form papillae only because they can more effectively utilize the available carbon sources than the Lac- cells from which they derive. Very much the same pattern is obtained by making up artificial mixtures of Lac+ and stable Lac- and inoculating from needle-points to lactose agar, (usually EMB).

This is not to say that all papillae arise by the same mechanism. In the case of the Reiner-Miller phenomenon (especially the rhamnose inhibitions) there may very well be both an "anaphragmic" (viz. Lwoff, Cold Spr. Harb. Symposium, 11, 1946) mutations, and direct effects of the rhamnose on sensitive cells. The existence of morphological novelties in inhibited colonies, which also show resistant papillae, may very well be interpreted however in terms of 1) a neomorphogenic effect of the rhamnose on sensitive cells, inhibited by the sugar, and 2) the spontaneous development of resistant mutants, not necessarily as a directed consequence of the morphological changes. I shall be most interested to read your findings on this point.

I should like to take this opportunity to confess some other experiments directly stimulated by your papers-- we have begun some experiments with Streptomyces griseus to determine whether a sexual phase can be verified by the same type of approach as we used with E. coli . I shall certainly keep you informed of any developments, but will welcome any suggestions you may have in the meantime.

Yours sincerely,

Joshua Lederberg